REMARKS

Claims 1, 3-17, 27 and 31-37 are pending in the present application. All of the claims were rejected in the final Office Action mailed on October 13, 2010. Claim 1 has been amended to specify that the present invention is directed to a "Biodegradable, linear, phase separated multiblock copolymer" and that both the soft biodegradable prepolymer (A) and the hard biodegradable prepolymer (B) are linear. Claim 1 has also been amended to further define the aliphatic chain extender as "a difunctional, aliphatic molecule." Support for these amendments is found in the specification at least at page 17, line 23 and page 14, lines 21-26. Thus, no new matter has been added by this amendment.

Applicants have carefully considered the final Office Action mailed on October 13, 2010 and respond to the specific issues raised therein as follows:

The Present Invention

The present invention is directed to biodegradable, phase separated segmented multiblock copolymers. By this amendment, the Applicants have further described the multiblock copolymers as "linear" in order to more clearly define what they believe to be their invention. The multiblock copolymers include segments of a linear soft biodegradable prepolymer (A) having a glass transition temperature (T_g) lower than 37°C and segments of a linear hard biodegradable prepolymer (B) having a melting point temperature (T_m) of 40-100°C. The prepolymer (A) segments and the prepolymer (B) segments are linked by a difunctional, aliphatic, multifunctional chain-extender and are randomly distributed in the copolymer.

Claim 1 has been amended to require that both the prepolymer (A) segments and the prepolymer (B) segments are linear and the chain extender is a difunctional, aliphatic, molecule. This combination of prepolymer (A) and (B) segments and the difunctional chain extender produces a linear multiblock copolymer—and not crosslinked copolymer structures. The specification discloses at page 14, lines 21-26 that:

> ***If the chain-extender is a difunctional, aliphatic molecule and the pre-polymers are linear***, a linear co-polymer is made; if one of the reactants (either the chain-extender or at least one of the pre-polymers) or both have more than two functional groups, cross-linked structures are obtained. Preferably, the chain-extender is an aliphatic di-isocyanate such as 1,4-butanediisocyanate.
>
> (Emphasis added.)

Maintained Rejections

Claim Rejections – 35 USC § 103

Claims 1, 3, 4, 9, 13, 14 and 31-37 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Application Publication No. US 2001/0009662 to Cohn et al. ("Cohn"). Cohn discloses polymeric compositions comprising the reaction product of a diol, diamine or dicarboxylic acid with a chain extender or coupling agent in about a 1:2 mole ratio. The resulting product is reacted with a monofunctional hydroxyl, amine or carboxylic acid containing compound to produce a pentamer. Cohn teaches the synthesis of multi-block copolymers having a controlled block distribution by using ACA blocks ***or*** a monofunctional block AB. This exclusively results in alternating block copolymers having uniform length.

Cohn teaches alternating multiblock copolymers

Cohn teaches alternating multiblock copolymers, instead of the random multiblock copolymers required by amended claim 1. A random multiblock copolymer in accordance with the present invention is, for example, represented by ABBBBBABAAABBAAAA… *etc.* An alternating multiblock copolymer according to the disclosure in Cohn on the other hand is, for example, represented by ABABABA… for the chain extension of AB prepolymers, or by ACAACAACAACA… for the chain extension of ACA prepolymers.

Based on the information regarding the constituents of the multiblock copolymer disclosed in Cohn, one of ordinary skill in the art would conclude that only alternating multiblock copolymers can be obtained and that multiblock copolymers with a random distribution of the segments cannot be obtained. The basis for such a conclusion is found in the teachings of Cohn as set forth in detail below.

Cohn discloses that ***either*** ACA or AB is chain extended. There is no teaching or suggestion by Cohn that ACA and AB can be chain extended concurrently to form a random multiblock copolymer having ***both*** ACA and AB blocks. In fact, one of ordinary skill in the art would find that Cohn teaches away from combining AB and ACA blocks in the same copolymer. Evidence for this can be found in the following sections:

- Paragraph [0092] in Cohn discloses that: "***a polymeric composition comprising AB diblocks*** ... ***or ACA triblocks,***" thereby specifically referring to the AB diblock and ACA triblock prepolymers in the alternative.

- Paragraph [0095] of Cohn states that: "*the present polymers preferably are based on polyester/poly(oxyalkylene)* ***ACA triblocks or AB diblocks***," again specifically referring to the AB diblock and ACA triblock prepolymers in the alternative.

- Paragraph [0096] of Cohn discloses that: "in the case of diblocks, these are coupled with difunctional chain extenders, in much the same way that triblocks are chain extended with the same chain extenders," without referring to an option for having chain extension between diblocks and triblocks.

- Paragraph [0112] of Cohn teaches that: "the product which is formed from the reaction of the chain extender, coupling agent or crosslinking agent *with the* ***ACA triblock or AB diblock***," again specifically referring to the AB diblock and ACA triblock prepolymers in the alternative.

Chain extension of AB diblocks only or, alternatively of ACA triblocks only, automatically leads to multiblock copolymers with either alternating AB diblocks and chain extender $(AB—Q)_n$, or alternating ACA triblocks and chain extender $(ACA—Q)_n$, respectively. In contrast to the AB diblocks or ACA triblocks taught by Cohn, the amended claims require two different linear blocks —A and B— that are distributed randomly over a linear polymer chain.

Furthermore, from the description of the ACA triblocks and the AB diblocks in Cohn, one of ordinary skill in the art would understand that A and C in ACA triblocks ***or*** A and B in AB diblocks are ***always covalently linked*** to each other prior to chain extension. This is clearly disclosed in the following teachings of Cohn:

- Paragraph [0125] of Cohn teaches that: "AB diblocks according to the present invention comprise a first polyester A block … ***covalently linked*** to a B block."

- Analogously, paragraph [0132] of Cohn teaches that: "polymers according to the present invention which comprise a first polyester A block ***covalently linked*** to a diol, diamine or dicarboxylic acid compound C block … which is, in turn, ***covalently linked*** to a second polyester A block."

- Paragraph [0141] states that: "The term 'crosslinked' or 'crosslinker' is used to describe agents which ***covalently bond*** the ***ACA triblocks or AB diblocks*** to other triblocks, diblocks or other moieties in the present polymers."

As a consequence of the covalent linking of the blocks, only the following alternating multiblock copolymers can be obtained by Cohn: $(ACA—Q)_n$ in the case of ACA triblocks and $(AB—Q)_n$ in the case of AB diblocks, wherein Q is the chain extender.

In contrast to the ACA triblocks and AB diblocks taught by Cohn, the different segments (selected from A and B) of the present invention are always chain extended with a chain extender to form a polymer with ***A and B distributed randomly*** over the polymer chain. Hence, there is always a chain extender between the different prepolymer segments A and B so that the segments are not linked together in a fixed order.

The paragraph at the bottom of page 7 of the Office Action states that: "Cohn expressly teaches in ¶ [0012] that the multiblocks may be polymerized through coupling or crosslinking of

the diblocks." As discussed in more detail below, claim 1 has been amended to clearly state that the multiblock copolymers are linear and, therefore, they cannot be crosslinked.

The use of chemically distinct polyester A blocks is not Obvious

The Office Action states that the claimed multiblock copolymers would have been obvious to a person of ordinary skill in the art in view of the properties of block "A" of the ACA triblock copolymer. The Office Action states on page 5 that:

> [I]t follows that the ordinary skilled artisan would have been highly motivated to use routine experimentation to polymerize chemically distinct polyester "A" blocks and link them aliphatically, in order to produce the instantly claimed multiblock copolymer chain.

The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 418, 82 USPQ2d 1385, 1396 (2007) noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Federal Circuit has stated that "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See also *KSR,* 550 U.S. at 418, 82 USPQ2d at 1396 (quoting Federal Circuit statement with approval). See MPEP § 2142.

The teaching or suggestion to make the claimed combination (or modification) and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Cohn neither teaches nor suggests using different types of "chemically distinct polyester 'A' blocks" to prepare a single multiblock copolymer as the claims require. Instead, Cohn ***teaches away*** from such an embodiment. Both the description and the Examples in Cohn, specifically refer to multiblock copolymers wherein only one type of "A" block is used for the AB diblock or the ACA triblock. Also in Examples 8 and 10, referred to in the Office Action, only a single type of A block is used. Moreover, these Examples utilize a macro chain extender prepared by reaction of polycaprolactone and hexamethylene diisocyanate for chain extension of a diblock. Similar to small chain extenders, the macro chain extender can only lead to alternating multiblock copolymers.

Thus, unless there is some suggestion or motivation in Cohn to form multiblock copolymers from ACA triblocks and AB diblocks, a *prima facie* case of obviousness cannot be established. Accordingly, it is respectfully submitted that there is no such suggestion or motivation in Cohn to form the biodegradable, linear phase separated multiblock copolymers set forth in the claims.

Monomeric/polymeric nature of A and B blocks

At page 8, the Office Action refutes the Applicants' arguments that Cohn fails to teach or suggest random polymer structures as required by the claims by stating that:

> It is understood that Applicants' invention is directed to a random, multiblock copolymer. However, contrary to Applicants' assertions, the Cohn reference defines ***both the "A" and "B" blocks*** as being ***either monomeric or polymeric***, thereby minimally suggesting randomness to the very nature of the diblock. (Emphasis added.)

The Office Action concludes that the possibility for "A" and "B" blocks in the AB diblocks to be "either monomeric or polymeric minimally" suggests a randomness of the diblock. Cohn teaches that "A" blocks can be "polymeric" (paragraph [0012] of Cohn]or "monomeric." This follows from paragraph [0012] of Cohn, which discloses that "A is a polyester unit derived from the polymerization of monomers." Cohn teaches that the "A" block is a polymer that is "derived from the polymerization of monomers," but does not teach that the "A" blocks can be formed by "unpolymerized" monomers. Paragraph [0017] of Cohn states that: "Z is derived from an amine- or hydroxyl-containing monofunctional [sic] monomeric or polymeric compound." One of ordinary skill in the art would understand that this means that Z was formed by polymerizing a monomeric or polymeric compound into a polymer. Paragraph [0099] of Cohn teaches that "the A block of the ACA triblocks of the present polymers … ranges in size from one monomeric unit … up to about 400 or more monomeric units …" "[R]ejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 at 988, 78 USPQ2d at 1336 (cited with approval in *KSR,* 550 U.S. at 418, 82 USPQ2d at 1396). There is absolutely no teaching or suggestion in Cohn to use monomeric and polymeric "A" or "B" blocks mixed up within one multiblock copolymer. Both the description and the Examples in Cohn only refer to multiblock copolymers wherein only a single type of "A"block and a single type of "B" block is used for the AB diblock. Therefore, without some teaching or suggestion in Cohn that random copolymers can be formed because the "A" blocks and the "B" blocks can be either monomeric or polymeric, there is no basis for

finding that it would be obvious to use different types of "A" and "B" blocks in a multiblock copolymer.

Cross-linking

The Office Action states in the paragraph at the bottom of page 7 that:

> Cohn expressly teaches in ¶[0012] that the multiblocks may be polymerized through coupling or crosslinking of the diblocks. It is further taught and suggested in the discussion of "crosslinking" at ¶[0141], that the already randomly defined di- and tri-block copolymers may be bound to other diblocks, triblocks and other moieties of the invention.

Paragraph [0141] of Cohn discloses polymers wherein diblocks and triblocks may be bound to other diblocks, triblocks and other moieties by a crosslinker. However, this does not lead to non-crosslinked multiblock copolymers or, in the alternative, to linear multiblock copolymers as defined in amended claim 1. The amended claims require a linear multiblock copolymer comprising segments of a linear soft biodegradable prepolymer (A) and segments of a linear hard biodegradable prepolymer (B) linked by a difunctional aliphatic chain extender. (See amended claim 1.) As the specification teaches at page 14, lines 21-26, the prepolymers cannot be cross-linked by a difunctional aliphatic chain extender and always form linear multiblock copolymers.

Paragraph [0141] of Cohn clearly states "as used herein, a crosslinker refers to a chemical compound which contains at least three (3) reactive moieties." Reaction of AB diblocks, or alternatively ACA triblocks, with such a crosslinker that has at least three reactive moieties will result in a ***thermosetting polymer*** with a 3-D network of bonds rather than a ***linear*** copolymer as required by amended claim 1. Accordingly, the amendment to claim 1, which requires the

copolymer to be linear, distinguishes the claims from the crosslinked copolymers taught by Cohn.

Combined use of AB and BA diblocks

The Office Action states at the bottom of page 7 that:

> Lastly, concerning Applicants' assertion pertaining to the order of the copolymer blocks, the Examiner maintains that an "A" block is not always or necessarily followed by either a "B" or "C" block, as evidenced by the foregoing discussion. It is possible, that an "AB" block may be followed by a "BA" block or an "ACA" block.

The Applicants respectfully submit that, in accordance with the teaching of Cohn, an AB diblock may be followed by a BA diblock. However, there is no teaching or suggestion in Cohn that an AB diblock can be followed by an ACA triblock. Cohn consistently teaches that the AB blocks and the ACA blocks are different embodiments. As already shown above, there is no disclosure or suggestion by Cohn that ACA and AB can be chain extended concurrently to a linear, random, multiblock copolymer having ACA and AB blocks.

When the AB diblock is difunctional with the same functional group, the following multiblock copolymers may be generated by chain extension with a difunctional chain extender, Q:

—AB—Q—BA—Q—BA—Q—BA—Q—AB—Q—AB—Q—BA—Q—

That is, AB may be followed by either BA or AB. However, this multiblock copolymer will have similar chemical properties as an alternating multiblock copolymer and, in fact, is not phase separated as required by amended claim 1.

As explained, in the Applicants' international publication at page 2, lines 23-29:

> The term "phase-separated", as used herein, refers to a system, in particular a copolymer, built of two or more different prepolymers, of which at least two are incompatible with each other at temperatures of 40° C. or below (when kept at body conditions). Thus the prepolymers do not form a homogeneous mixture when combined, neither when combined as a physical mixture of the prepolymers, nor when the prepolymers are combined in a single chemical species as "chemical mixture", viz. as copolymer.

The above polymer disclosed by Cohn is not built of two or more ***different prepolymers*** because the prepolymer AB is clearly identical to the prepolymer BA. Moreover, in the above described multiblock copolymer, it is not possible to have large distinct A and B domains, illustrating that this is not a phase-separated multiblock copolymer.

New Claim Rejections – 35 USC § 103

Claims 5-8, 10-12, 15-17 and 27 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Cohn in combination with U.S. Patent No. 5,066,772 to Tang et al. ("Tang"), which discloses copolymers of recurring units. The teachings of Cohn and how they are distinguishable from the claims of the present invention are discussed above in detail. With regard to Tang, the Office Action states in the middle of page 9 that:

> Tang et al. [] expressly defines random copolymer fabrication in terms of both the "A" and "B" block (col. 7, line 59 to col. 8 line 33). Of particular note is that the components of each block may comprise a single type of recurring monomeric unit or, alternatively, each may comprise multiple type of recurring monomeric unit, ***randomly distributed throughout each block*** (col. 8, lines 10-15).
>
> (Emphasis added.)

The specific teaching cited in the Office Action is found at col. 8, lines 4 to 13 of Tang and states that:

> As used herein, the term "block" means a sequence of one type of monomeric unit at least about 5 monomeric units long, or such sequence of two or more types of ***recurring monomeric units either randomly distributed in such a sequence*** or distributed such sequence in a block-like fashion. Each "A" block and "B" block may comprise a single type of recurring monomeric unit. Alternatively, each block may comprise more than one type of recurring monomeric unit, ***randomly distributed throughout each block***.
>
> (Emphasis added.)

Amended claim 1 requires a ***linear copolymer*** and the last line requires "prepolymer (A) and the segments of the hard biodegradable prepolymer (B) [to be] ***randomly distributed in the copolymer***." (Emphasis added.) The ***random distribution*** taught by Tang is ***not in the copolymer*** but in the blocks that are used to form the copolymer. The definition of the term "block" as it is defined above in Tang states that the block can be made up of: "***recurring monomeric units . . . randomly distributed.***" The Office Action confirms this when it states (as cited above) that the monomeric units are "***randomly distributed throughout each block.***"

One of ordinary skill in the art would not find the ***random distribution of blocks in a copolymer*** required by the present claims obvious in view of the ***random distribution of monomeric units in a block taught by Tang***.

Tang describes copolymers for use in the fabrication of a medical device. As clearly indicated by Tang, these copolymers are either random copolymers, or in the alternative block copolymers (col. 7, lines 59-62). Tang does not describe random multiblock copolymers as provided by the present invention. The block copolymers disclosed in Tang have repeating block units (col. 8, lines 14-20). The nature of randomness as required by the present invention implies that the copolymer does not possess a repeating block unit as described in Tang. Since

the block copolymers mentioned in Tang possess reoccurring repeating blocks they are in fact ordered block copolymers, rather than random block copolymers. The random copolymers in Tang, on the other hand, have a complete random sequence of monomeric units, and lack defined blocks. Therefore, Tang only teaches random copolymers, rather than random block copolymers (e.g., col. 7, line 60; col. 8, line 37; col. 9, lines 4-5, 7-8 and 14; and col. 13, Example 4). Moreover, in the present invention the fabrication of a phase separated multiblock copolymer with random distribution of the segments is enabled by the use of a multifunctional chain extender, which is absent in the copolymers taught by Tang.

Distinguishing characteristics of the linear, random, multiblock copolymers in the Claims

The linear, random, multiblock copolymers of the present invention provide many advantages that cannot be obtained with alternating multiblock copolymers.

First, the random multiblock copolymers obtained by chain extension of A and B blocks have unlimited A to B ratio. A:B can, for instance, be 10:90, but may as well be 90:10. In contrast, the ratio of the blocks in an alternating multiblock copolymer is limited to the ratio used in the chain extended polymer. For instance, in the case of chain extension of AB the A:B ratio in the multiblock copolymer is 50:50. The random nature of the multiblock copolymers of the present invention greatly increases the possible compositions of the material and thereby the control over its physical and chemical properties. This includes more control over the swelling capacity in water, morphology (phase separation, amorphous/crystallinity) and polymer degradation.

Second, the synthesis method of the random multiblock copolymers of the present invention is much less laborious as compared to the synthesis of alternating multiblock copolymers. In alternating multiblock copolymers, either segment A and B in case of AB diblocks (or either segment A and C in case of ACA triblocks) have to be linked prior to chain extension (or a macro chain extender needs to be synthesized). In accordance with the present invention, separate A and B blocks are chain extended with, e.g., a commercially available chain extender.

Page 15 of the Office Action states that col. 8, lines 20-33 of Tang either teaches or suggests blocks that are randomly distributed in a copolymer. The cited disclosure in Tang reads as follows:

> Alternatively, the various "A" and "B" blocks contained in the block copolymers may have more than one type of "A" block or "B" block, each of which may contain a different type or types of recurring monomeric units; or each block may contain the same or different types of recurring units but have differing number of recurring units in each block. With respect to the ***recurring blocks*** of A's and B's, each of them may also be the same or different. For example, ABABA may in fact be MNOPQ, ABA may be MNQ or ABA may be MNOPQ, where M, N, O, P and Q are the same or different provided that *at least one of M, N, O, P and Q is a* ***recurring unit*** of the Structure I or II.

Tang teaches that the recurring blocks "may also be the same or different" and that at least one of the blocks "is a recurring unit of the Structure I or II." The Applicants respectfully submit that one skilled in the art would find the teaching of recurring blocks in a copolymer structure to teach away from a random copolymer as required by the claims. There is no teaching or suggestion in Tang that the blocks in a multiblock copolymer can be ***both random***

and recurring. The word recurring used by Tang to describe the copolymers implies that they are non-random and have a predictable structure.

Conclusion

Applicants submit that the amendment to claim 1 and the arguments made herein clearly distinguish the cited prior art and respectfully request allowance of the claims.

If the Examiner has any questions relating to this Amendment, the Examiner is respectfully invited to contact Applicants' attorney at the telephone number provided below.

Respectfully submitted,

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